

- (ii) a mismatched complex immobilized to the substrate, the complex comprising the first nucleic acid and a second nucleic acid having a single nucleotide mismatch;

is not decreased compared to the difference in  $T_m$  between the complexes in low immobilization density.

7. (Once amended) The substrate of claim 1 wherein the high immobilization density comprises oligomers on the substrate so that the ratio ( $r_s$ ) of the mean centre-to-centre separation distance of the oligomers to the average length of immobilized oligomers is less than or equal to 1.7.
- 
16. (Once amended) A substrate of claim 1 wherein a plurality of first nucleic acids and a plurality of one or more oligomers that are not nucleic acids are immobilized on the substrate.
21. (Once amended) The substrate of claim 1 wherein the interfacial hybridization for fully complementary nucleic acids exhibits enhanced sensitivity to temperature.
22. (Once amended) The substrate of claim 1 wherein the substrate comprises an optical fiber, an optical wave-guide, a spot on a microarray chip, a microtiter plate well, a metal film for surface plasmon resonance determination, a glass bead, a planar waveguide, a quartz oscillator, a ceramic oscillator, a conductive electrode material, a semi-conductive electrode material, a plastic sample compartment, an optical component, or a pyroelectric material.
32. (Once amended) The method of claim 25 wherein the substrate comprises an optical fiber, an optical wave-guide, a spot on a microarray chip, a microtiter plate well, a metal film for surface plasmon resonance determination, a planar waveguide, a quartz oscillator, a ceramic oscillator, a conductive electrode material, a semi-conductive

electrode material, a glass bead, a plastic sample compartment, an optical component, or a pyroelectric material.

33. (Once amended) A method of hybridizing nucleic acids comprising:
- (i) providing a substrate including a plurality of first nucleic acids or first nucleic acids and oligomers which are not nucleic acids on the substrate, having a medium-high or high immobilization density; and
  - (ii) contacting the substrate with at least one second nucleic acid having a region of contiguous nucleotides that are complementary to all or part of at least one of the first nucleic acids, so that the second nucleic acid hybridizes to the at least one first nucleic acid.
37. (Once amended) The method of claim 33 wherein the second nucleic acid and the at least one first nucleic acid hybridize in a high ionic strength solution.
43. (Once amended) The method of claim 35 wherein the first nucleic acids comprise a mixture of nucleic acid sequences.
44. (Once amended) The method of claim 33 wherein the substrate comprises an optical fiber, an optical waveguide, a spot on a microarray chip, a microtiter plate well, a metal film for surface plasmon resonance determination, a planar waveguide, a quartz oscillator, a ceramic oscillator, a conductive electrode material, a semi-conductive electrode material, a glass bead, a plastic sample compartment, an optical component, or a pyroelectric material.

46. (Once amended) The method of claim 33 further comprising a step of detecting hybridization.

48. (Once amended) A method of detecting the presence of a genetic target in a test sample, comprising:

- (i) providing a substrate including a plurality of genetic marker nucleic acids immobilized to the substrate, alone or in combination with one or more oligomers at a medium-high or high immobilization density;
- (ii) contacting the substrate with a test sample comprising a mixture of nucleic acids so that a second nucleic acid having a region of contiguous nucleotides that are complementary to all or part of at least one of the genetic marker nucleic acids hybridizes to at least one first nucleic acid; and
- (iii) detecting hybridization of the genetic marker to the second nucleic acid, wherein hybridization is indicative of the presence of a genetic target in the sample.

50. (Once amended) The method of claim 48 wherein, in an assay, the difference in  $T_m$  between

- (i) a fully-matched complex immobilized to a substrate, the complex comprising the first nucleic acid and the second nucleic acid; and
- (ii) a mismatch complex immobilized to a substrate, the complex comprising the first nucleic acid and a second nucleic acid having a single nucleotide mismatch;

is increased or maintained relative to the difference in  $T_m$  between the complexes in low immobilization density.

55. (Once amended) The method of claim 48 wherein the hybridization for fully complementary nucleic acids exhibits enhanced sensitivity to temperature.
- 
58. (Once amended) The method of claim 50 wherein the first nucleic acids comprise a mixture of nucleic acid sequences.
59. (Once amended) The method of claim 48 wherein the substrate comprises an optical fiber, an optical waveguide, a spot on a microarray chip, a microtiter plate well, a metal film for surface plasmon resonance determination a planar waveguide, a quartz oscillator, a ceramic oscillator, a conductive electrode material, a semi-conductive electrode material, a glass bead, a plastic sample compartment, an optical component, or a pyroelectric material.
62. (Once amended) The method of claim 48 wherein the genetic marker nucleic acids are derived by a nucleic acid amplification method.
63. (Once amended) The method of claim 48 wherein the genetic target comprises an environmental marker nucleic acid, a food marker nucleic acid or a biowarfare agent nucleic acid.
67. (Once amended) The method of claim 48 wherein the nucleic acids to be tested comprise an indicator agent.
75. (Once amended) A method for identifying or isolating a target nucleic acid from a mixture containing nucleic acids which comprises the steps of:

- (i) providing a substrate of claim 1 wherein the first nucleic acids comprise a sequence that is complementary at least in part to the target nucleic acid; and
  - (ii) contacting the substrate with the mixture containing nucleic acids such that any target nucleic acid present in the mixture can hybridize to the first nucleic acids on the substrate.
76. (Once amended) The method of claim 75 wherein the step of contacting the substrate with the mixture is performed at high ionic strength.
77. (Once amended) The method of claim 75 wherein the mixture containing nucleic acids can contain nucleic acids that differ from the target nucleic acid by a single base change.

#### In the Specification

At page 1, lines 13-21, please replace the third full paragraph with the following:

--The immobilization of biomolecules to solid surfaces is widely used in the preparation of analytical sensors. Applications include immunosensor techniques (R. Blonder, E. Katz, Y. Cohen, N. Itzhak, A. Riklin, I. Willner, *Anal. Chem.*, v. 68, p. 3151, 1996; R. Granzow and R. Reed, *Biotechnology*, v. 10, p. 390, 1992; B. König and M. Grätzel, *Anal. Chim. Acta*, v. 309, p. 19, 1995), which tend to rely on protein binding as the means of molecular "recognition", as well as those which make use of nucleic acid hybridization [K.M. Millan, A. Saraullo, and S.M. Mikkelsen, *Anal. Chem.*, v. 66, p. 2943, 1994; J. Wang, S. Bollo, J.L. Lopez Paz, E. Sahlin and B. Mukherjee, *Anal. Chem.*, v. 71, p. 1910, 1999; H. Su, K.M.R. Kallury, M. Thompson and A. Roach, *Anal. Chem.*, v. 66, p. 769, 1994; F. Caruso, E. Rodda, D.N. Furlong, K. Niikura, and Y. Okahata, *Anal. Chem.*, v. 69, p. 2043, 1997; A.P. Abel, M.G. Weller, G.L. Duveneck, M. Ehrat and H.M. Widmer, *Anal. Chem.*, v. 68, p. 2905, 1996; P.A.E. Piunno, U.J. Krull, R.H.E. Hudson, M.J. Damha and H. Cohen, *Anal. Chem.*, v. 67, p. 2635, 1995] as the basis for selective recognition. The use of immobilized nucleic acids to provide for selective binding interactions is attractive since the selectivity of nucleic acid binding interactions can be quite high and the advent of polymerase chain reaction and solid phase nucleic acid synthesis has allowed for relatively simple nucleic acid preparation and immobilization.--